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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,296	03/22/2004	Jaime A. Rabi	IDX1012C	1836

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EXAMINER	
KRISHNAN, GANAPATHY	
ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/806,296	RABI, JAIME A.	
	Examiner	Art Unit	
	Ganapathy Krishnan	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-20 and 69-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-20 and 69-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 4/12/2007 has been received, entered and carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1-12, 21-68 have been canceled.

2. Claims 13 and 17 have been amended.

3. Remarks drawn to objection to drawings and rejections under 35 USC 112, second paragraph and 103.

Claims 13-20 and 69-85 are pending in the case.

Drawings

The objection to drawings has been overcome by filing of replacement sheets with appropriate corrections.

The following rejection under 35 USC 112, first paragraph is made of record necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-20 and 69-85 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had full possession of the claimed invention.

The claims herein are drawn to a process for the preparation of an optionally protected β-L-2'-deoxythymidine, wherein one of the process steps (step (c)) involves reacting an optionally protected L-1-O-alkyl-2-deoxyribose with an acyl halide that generates an anhydrous acid halide (acid halide defined in the specification as including HCl) in situ to form an optionally protected L-1-halo-2-deoxyribose.

The specification as originally filed does not provide adequate support for the process step (c) in instant claim 13. According to the recitation of process step (c), in claim 13, inorder to generate the acid halide in situ the acyl halide has to react with the said L-1-O-alkyl-2-deoxyribose containing a free hydroxyl group to generate the acid halide, HCl in this case. Since step (c) in claim 13 recites the terms optionally protected, the said step may involve an unprotected L-1-O-alkyl-2-deoxyribose (deoxyribose with free hydroxyl group). According to the recitation in step (c) of claim 13, the desired product, namely, the L-1-halo-2-deoxyribose is formed by the reaction of an acyl halide with the said L-1-O-alkyl-2-deoxyribose and also generates the acid halide in situ. According to Figure 3 (in replacement sheet 2) it is the L-1-methoxy-3,5-ditoluoyl-deoxyribose that is depicted as reacting with an acyl halide to form the desired L-1-halo-2-deoxyribose. Since the L-1-methoxy-3,5-ditoluoyl-deoxyribose has all of its hydroxyl groups protected, it cannot generate the acid halide (HCl) in situ as recited. Example 3 at pages 60-61 of the specification also teaches the reaction of the totally protected 2-deoxyribose reacting with acetyl chloride (acyl halide) to form the chlorosugar. Even though the prior step in Figure 3, shows the reaction of 1-methoxy-2-dexoyribose reacting with p-toluylchloride to from the ester, which would generate the said acid halide in situ, this reaction

does not produce the L-1-halo-2-deoxyribose as recited in step(c) of claim 13. It produces a protected deoxyribose.

One of ordinary skill in the art would clearly recognize that the process as described in example 3 and as depicted in figure 3, does not generate acid halide and also form the halo-2-deoxyribose in the same step, as recited step (c) in claim 13.

Thus, the claimed recitation is seen to clearly lack written description.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claims 13-20 and 69-85 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been overcome in view of applicants arguments and reference to the specification for definitions.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of Claims 13-20 and 68-85 under 35 U.S.C. 103(a) as being unpatentable over Gosselin et al (US 6,444,652, '652 patent) in combination with Weis et al (WO 96/13512) is being maintained for reasons of record.

Applicants' have traversed the rejection by arguing that:

1. Gosselin does not disclose the conversion of 1-O-alkyl-ribose to a halide before reacting it with a silylated base, as admitted by the Office.

2. Weis, in Scheme IV discloses structure 29 which merely has a chlorine at the 2-position of the ribose and not at the 1-position as recited in instant claims 13 and 17 and also HCl is added and not generated in situ.

In view of the above the instant invention is not rendered obvious according to the applicants. Applicants' arguments are not found to be persuasive.

Gosslein et al ('652) teaches the reaction of silylated uracil with a protected ribose sugar in dichloroethane to give the nucleoside 10, which is then deprotected (cols. 25-26, scheme at the bottom half of the page). The ribose sugar that is reacted with the silylated uracil is obtained from L-ribose by treatment of L-ribose with methanol and acid followed by protection of the hydroxyl groups with benzyl chloride in the presence of pyridine (base, acid scavenger; col. 19, Reaction 1). Hence, the reaction steps of forming 1-O-alkyl-ribose by reaction of a ribose with methanol and protection of the remaining free hydroxyl groups and its coupling to uracil via the silylated derivative and subsequent deprotection of the protecting groups is taught by Gosselin. Even though the reactions above are performed with a ribose, one of ordinary skill in the art will recognize that the same reaction can be performed with a deoxyribose too.

Weis et al, drawn to preparation of ribofuranosyl nucleosides, teaches the reaction of a silylated base with a ribose sugar that has a chlorine at the 1-position to give the corresponding nucleoside is performed using mild conditions and goes to completion in 2hours (page 13, Scheme IV, not structure 29 as pointed out by applicants), whereas the same type of coupling with the ribose sugar having oxygenated leaving group (OAc in this case) takes 16 hours to go to

completion (page 9, Scheme II). One of ordinary skill in the art will recognize from this teaching that having a halide at the 1-position of the ribose ring (as instantly claimed) speeds up the coupling step with the silylated base.

Whether an acid halide is generated in situ or not, the end product produced is the same. At page 20, Weis teaches the conversion of structure 55 (protected deoxyribose) to the 1-halo derivative (structure 56). Structure 55 is produced from structure 54 via reactions as instantly claimed (as seen in Figure 3). Even though the halodeoxyribose in the reaction scheme of Weis is formed by the reacting with added HCl it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute HCl with another source of halogen like an acyl halide in a process for the preparation of the 1-halo-2-deoxyribose and beta-L-2'-deoxythymidine and beta-L-2'-deoxyuridine as instantly claimed, since the process steps and reagents for the desired products is seen to be taught in the prior art using the structurally close ribose sugar and analogous reagents. Irrespective of whether an acid halide is generated in situ or not the end result is the formation of the halosugar.

One of ordinary skill in the art would be motivated to use the process as instantly claimed since the process is mild and step wherein the ribose containing the halide at the 1-position is coupled to the silylated base is fast compared to the same step wherein the ribose has an oxygenated leaving group. A reaction step that is art tested to be fast and yields the desired product in high yield is preferable. The skill artisan also knows that the reaction sequence performed with a ribose will also work equally well with a deoxy ribose. One of skill in the art would also be motivated to substitute HCl with other sources of halogen like acyl halides for the halogenation step in order to optimize yields of the halosugar.

Conclusion

Claims 13-20 and 69-85 are rejected

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

GK

6/20/07

Shaojia Jiang
Supervisory Patent Examiner
Art Unit 1623